Non-Technical Abstract

Infection with the human immunodeficiency virus (HIV), the virus associated with the Acquired Immunodeficiency Syndrome (AIDS), is often characterized by gradual impairment of the immune system leading to increased infections and an increased risk for the development of cancers, including lymphoma, a cancer of the lymph node cells. Drug therapy such as zidovudine (AZT) may temporarily slow the progress of HIV infection, but the disease usually progresses to a fatal immunodeficiency. Lymphomas in patients with HIV infection are usually treated with chemotherapy or radiation therapy which may provide a temporary remission, but recurrence of the cancer is common. This study is evaluating bone marrow transplantation as a therapy for both the lymphoma and HIV infection. Prior to bone marrow transplant very high doses of chemotherapy combined with total body irradiation (TBI) can be given in an attempt to destroy the lymphoma cells. This treatment will also destroy the normal bone marrow and the blood cells infected with HIV. Donor bone marrow will be given to replace the destroyed marrow. In an attempt to prevent HIV infection of the donated bone marrow and destroy any residual HIV infected cells, we will boost immunity to HIV with a treatment called adoptive immunotherapy.

Most patients with HIV initially develop some immunity to the virus provided by lymphocytes which specifically recognize and kill HIV infected cells. The presence of these cells in the body appears to help prevent HIV spread and progression to AIDS. The chemotherapy and radiation therapy used to destroy the lymphoma cells will also destroy the lymphocytes providing this immunity to HIV. Therefore, we will attempt to isolate these specific lymphocytes that fight HIV from the patient's blood before the bone marrow transplant and grow these cells to large numbers in the laboratory. These lymphocytes will be given back to the patient after the transplant in an attempt to provide immunity to HIV and prevent the virus from infecting the new immune system developing from the donated marrow. We will insert a gene into the lymphocytes to be used in immunotherapy to provide a sensitive indicator of the survival of these cells after giving them back to the patient. Since this is a new experimental therapy, it is possible the transferred lymphocytes might cause side effects due to inflammation initiated when these cells contact residual HIV infected cells. Therefore, the gene inserted into the lymphocytes, termed HyTK, was selected to make a protein that will kill the cells if they are exposed to the drugs acyclovir or ganciclovir (used to treat herpes and cytomegalovirus infections). The presence of this gene in the transferred lymphocytes should allow us to destroy them if they cause any serious side effects by administering ganciclovir. If the cells do not cause any side effects at all, but ganciclovir or acyclovir are required to treat a herpes virus infection developing after transplant, we will administer lymphocytes that were not modified by the gene transfer technique.